QT Dispersion in Adult Hypertensives

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Increased QT dispersion is associated with sudden cardiac death in congestive cardiac failure, hypertrophic cardiomyopathy and following myocardial infarction. Patients with hypertension—in particular, those with left ventricular hypertrophy (LVH)—are also at greater risk of sudden cardiac death. We examined whether QT dispersion, which is easily obtained from a routine ECG, correlates with LVH. One-hundred untreated patients with systemic hypertension and 78 normotensives had QT dispersion measured manually from a surface 12-lead electrocardiogram and two-dimensional echocardiography performed to measure interventricular septal thickness, posterior wall thickness and left ventricular internal diameter. Office blood pressure was also recorded. Multivariate analysis demonstrated significant relationships between QT dispersion and office systolic blood pressure, and left ventricular mass index. Manual measurement of QT dispersion might be a simple, noninvasive screening procedure to identify those hypertensives at greatest risk of sudden cardiac death in a third-world country.

Key words: systemic arterial hypertension ■ QT dispersion ■ left ventricular hypertrophy

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INTRODUCTION

Hypertension affects the heart and the arterial tree in many ways. One such effect is ;eft ventricular hypertrophy (LVH).[1] Long-standing hypertension, after leading to cardiac hypertrophy and enlargement, will manifest radiologically as an increase in cardiothoracic ratio (CTR),[2] and electrocardiographically as LVH.[3] A number of studies have suggested that hypertension plays a disproportionate role in increasing the risk of sudden cardiac death.[4] The principal mechanism by which hypertension predisposes to sudden cardiac death is via left ventricular hypertrophy.[4] It is well recognized that hypertensive LVH is associated with excess fibrous tissue deposition throughout the myocardium, and thus they have a higher propensity to development of ventricular arrhythmias than patients without LVH or normotensives.[4-6] The potentially dangerous ones include couplets, ventricular tachycardia and fibrillation, which may terminate in sudden cardiac death.[5,6] QT interval prolongation has been found to predict sudden cardiac death in patients with chronic ischemic heart disease,[7] hypertensive heart disease,[8] sickle cell anemia patients[9] and even apparently healthy individuals.[10] However, recent interest has focussed on interlead QT variability (QT dispersion) as a possible predictor of sudden cardiac death.[11-13] Patients with congestive heart failure,[14] acute myocardial infarction[15] and hypertrophic cardiomyopathy[16] who die suddenly have been demonstrated to have increased QT dispersion. Increase in QT dispersion is an electrocardiography measure of ventricular repolarization and also a risk marker for ventricular tachyarrhythmias.[8,9,11-14] If this hypothesis is correct, measurement of QT dispersion might be a simple, noninvasive screening procedure to identify hypertensive patients who may be at increased risk of sudden cardiac death. This study was undertaken in view of the paucity of information on QT dispersion in Nigerians with systemic hypertension. We aimed to assess the relation between QT dispersion and blood pressure, and LVH in these hypertensives.

Patients and Methods

One-hundred newly diagnosed hypertensives who have never been on antihypertensive therapy, compared with 78 sex- and age-matched healthy controls, were studied. Exclusion criteria include diabetes mellitus, stroke and/or renal insufficiency; concomitant cardiovascular disease, e.g. rheumatic valvular heart disease; sickle cell anemia; ischemic heart disease; or corpulmonale. Also excluded are those with packed cell volume (PCV) of <30%, significant alcohol consumption of >100 g/day and/or cigarette smoking of >5 sticks per day. Serum albumin of <3 g/100 ml, failure to give consent and/or history of any drug known to prolong QT interval were excluded. Arterial blood pressure was measured from the dominant arm of all the subjects. Three readings were taken with a five-minute interval and averaged to give the office systolic and diastolic blood pressures. Patients are then classified according to the World Health Organization/International Society of Hypertension classification of 1999.[17] The weight (kilograms) was recorded to the nearest 0.5 kg, and height (meters) was measured with a rigid measure against a vertical wall. The body mass index (BMI) was then calculated using the formula: BMI = Wt (kg)/Ht $(m)^2$ and expressed as kg/m^2.[18] The waist circumference (centimeters) was measured with a tape at the level of the umbilicus on the unclothed abdomen and the hip circumference (centimeters) measured at the level of external margins of the anterior superior iliac crests. The mean of two readings was taken in each case for waist-to-hip ratio determination. Urinalysis and chest x-ray (PA) view were also done on each subject. A standard 12-lead resting echocardiogram (ECG) was recorded at 25 mm/s and 1 mV/cm standardization using the Schiller Cardiovit AT-1 three-channel machine. The QT interval (QTo) was manually measured in all 12 leads of the ECG and corrected for heart rate using the formula of Hodges et al.[19] (QTc = QTo + 1.75 (ventricular rate – 60). At least three consecutive cycles were measured for each lead and averaged as reported by other workers.[11,12] Corrected QT dispersion (QTd) defined as (QTd max – QTd min) was then calculated. Adjusted QT dispersion (QT dispersion / number of leads$^{1/2}$) was also measured to correct for the known dependence of the index on the number of measured leads.[20] ECG left ventricular hypertrophy (ECG LVH) was determined using Araoye's proposed criteria for LVH in black hypertensives.[21] Echocardiographic examination was performed with ALOKA SSD 1700 using a 3.5-MHz transducer. According to the Penn convention, two-dimensional measurements were taken of interventricular septal wall thickness (IVSD), posterior wall thickness (PWT) and left ventricular internal diameter (LVID) at end of diastole in a parasternal long axis view at the level of the mitral valve tips. Left ventricular mass (LVM) was then calculated according to the formula of Devereux and Reichek[22] and then indexed to body surface area to give left ventricular mass index (LVMI).

Statistical Analysis

Quantitative variables were reported as mean ± SD and nonquantitative as percentages. Chi-squared and Student's t tests were used where applicable, to compare quantitative variables between subjects and controls. Pearson's correlation coefficient analysis was performed and variables that demonstrated significant positive relationship to QT dispersion were then entered into a stepwise multiple regression analysis. The level of statistical significance in each case was taken as $P<0.05$.

RESULTS

The demographic characteristics of the study

Table 1. Study group characteristics

	Hypertensive	Control	P Value	Hypertensive	Control	P Value
Sample size	61	46		39	32	
Mean age (years)	51.7 ± 11.5	53.0 ± 11.2	0.27	50.8 ± 11.9	49.0 ± 11.8	0.28
BMI (kg/m^2)	23.2 ± 3.9	22.5 ± 2.8	0.13	26.7 ± 5.7	23.5 ± 3.6	0.003
WHR	0.96 ± 0.07	0.92 ± 0.04	0.0001	0.95 ± 0.09	0.85 ± 0.03	0.005
SBP (mmHg)	181.4 ± 33.0	125.7 ± 10.0	0.0007	187.0 ± 28.0	123.0 ± 11.0	0.004
DBP (mmHg)	116.7 ± 21.0	79.2 ± 6.0	0.0001	117.0 ± 23.0	79.0 ± 6.0	0.004
CTR	0.58 ± 0.08	0.48 ± 0.04	0.0001	0.61 ± 0.08	0.49 ± 0.03	0.003
RI	10.4 ± 4.8	9.1 ± 2.9	0.05	11.6 ± 4.7	9.5 ± 3.1	0.03
SV2+RV6	43.1 ± 11.9	28.2 ± 8.1	0.007	37.2 ± 3.9	25.0 ± 6.1	0.004
QTD (ms)	54.6 ± 9.7	15.1 ± 10.3	0.0003	51.9 ± 8.5	17.5 ± 12.7	0.0002
Adjusted QTD (ms)	25.9 ± 12.8	4.6 ± 3.3	0.0001	23.9 ± 10.6	5.6 ± 4.3	0.0004
LVM (g)	305.0 ±138.0	173.9 ± 14.0	0.0009	269.3 ± 115.0	154.0 ± 51.0	0.0003
LVMI (g/m^2)	180.2 ± 90.0	96.4 ± 29.0	0.0001	173.8 ± 71.0	88.7 ± 28.0	0.0004

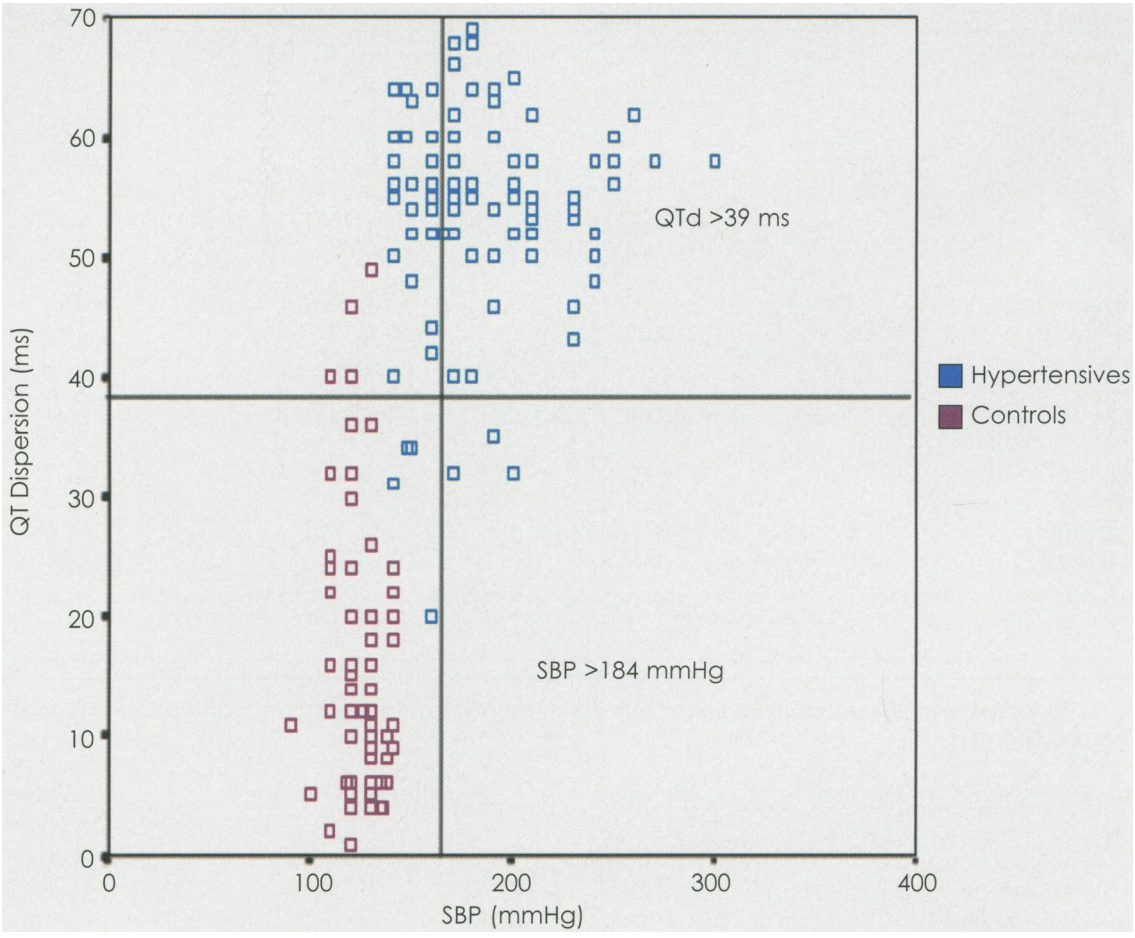
P value <0.05 (statistically significant); BMI: body mass index; WHR: waist-to-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; CTR: cardiothoracic ratio; R1: R amplitude in limb leads 1; SV2 + RV6: sum of S amplitude in chest lead 2 plus R amplitude in 6; QTD: QT dispersion; LVM: left ventricular mass; LVMI: left ventricular mass index

group are as shown in Table 1. The age range of the study population was 30–80 years. More than 53% were in the fifth decade. The hypertensives were generally more overweight than the controls, with mean BMI of 24.6 ± 5.0 kg/m² and 22.9 ± 3.0 kg/m² (p=0.003), respectively. Radiologic cardiomegaly (CTR >0.55) was found in 73% of the hypertensive subjects. Fifty-seven percent of the hypertensive patients had evidence of ECG LVH by voltage criteria, compared to only 6% in the controls (P=0.003). Seventy-one percent had ECG LVH compared to 7% in the controls (P = 0.007). Ninety-two percent of the hypertensives had increased QT dispersion above 39 ms, compared to 8% in the controls. Table 2 summarizes the correlation between QT dispersion and adjusted QT dispersion with other variables. Significant correlation existed between QT dispersion and CTR, ECG LVH, SBP, DBP, MAP, LVPW, LV mass and LVMI. Multiple linear regression analysis (Table 3), which adjusts each correlation for the others, revealed the most significant relationship to QT dispersion were SBP (P=0.003), LVM (P=0.005) and LVMI (P=0.004). Similar relationships were evident for adjusted QT dispersion. Figures 1 and 2 show that the majority of the patients with severe hypertension and LVH (>60%), had QT dispersion >39 ms.

DISCUSSION

Our findings demonstrate that increased QT dispersion on the 12-lead ECG is found in those hypertensive patients with more severe disease, i.e., those with the greatest LVMI and blood pressure. This is confirmed by the significant positive relationship between grades-II and -III hypertension with LVH and QT dispersion. Age, LVH and the presence of hypertension are independent predictors of ventricular arrhythmias.[3,5,6,8] More than 50% of our patients were in their fifth decade of life, had ECG and ECG LVH, and had a more severe form of hypertension, making them more vulnerable to the risk of developing any of the repolarization-related ventricular arrhythmias and therefore sudden cardiac death. This finding was similarly reported by Clarkson et al.,[12] while Mayet et al.[23] observed a significant correlation of the "lead-adjusted" QT dispersion with

Figure 1. Relationship between QT dispersion (ms) and SBP (mmHg)



left ventricular mass index in their patients. We also observed that 8% of our patients had a normal QT dispersion. Antihypertensive therapy has been shown to cause regression of left ventricular hypertrophy, but the effect on left ventricular fibrosis is not as well documented.[24,25] Therefore, this may alter the natural relationship between fibrosis and LV mass and, thus, may explain our observation. In addition, we have found that 7% of our controls have an increased QT dispersion of >39 ms. These controls had a normal blood pressure, left ventricular mass and no evidence of left ventricular hypertrophy either electrocardiographically or by echocardiography. This observation may therefore mean that either there is congenital long-QT interval syndrome within the population studied or we are seeing the effect of drug(s) that might have proarrhythmic effect not volunteered. The latter is highly unlikely, because none of them had history of recurrent syncope; family history of childhood sudden cardiac death or congenital deafness and the QT dispersion value is far less than that reported for patients with this syndrome (>100 ms).[12] The former may likely explain our finding because getting correct and accurate information is fairly difficult in our society, largely to due to ignorance. These controls might have used some of the drug(s) known to prolong QT interval such as antimalarials (especially halopanthrine), antibiotics and or antihistamines. However, determination of serum levels may have solved the problem. Regrettably, even this is lacking in our country. In any way, the incidence of drug-induced torsades de pointes has been reported to be low,[3] but as the list of drugs that can cause acquired long-QT syndrome is ever increasing, this may pose a real and serious concern to the medical community like ours. Echocardiography has been shown to be a very important noninvasive diagnostic tool, but its use in screening all hypertensives for LVH may not be possible, especially in a developing country such as ours, due to cost. From our data, we suggest that only patients with QT dispersion of 39–69 ms may require echocardiography (ECHO) for LVH detection, because only 4% with ECG LVH had QT dis-

Table 2. Pearson's correlation coefficient (r) between QTd, patient demographics, BP, ECG LVH and echocardiographic parameters

Parameters	QTD (ms)	P Value	Adjusted QTD (ms)	P Value
Age (years)	0.053	0.30	0.040	0.35
Height (cm)	0.036	0.36	0.004	0.49
Weight (kg)	-0.078	0.22	-0.201	0.02*
BMI (kg/m^2)	-0.096	0.17	-0.196	0.03*
WHR	-0.016	0.44	-0.035	0.37
CTR	0.189*	0.03*	0.189*	0.03*
ECG LVH	0.192**	0.03**	0.071	0.24
SBP (mmHg)	0.242**	0.008**	0.108	0.14
DBP (mmHg)	0.255**	0.005**	0.121	0.12
MAP (mmHg)	0.272**	0.003**	0.130	0.10
IVSd (cm)	0.170	0.05	0.024	0.41
LVIDd (cm)	0.150	0.07	0.183*	0.03*
LVPWd (cm)	0.217*	0.02*	0.117	0.12
LVM (g)	0.362***	0.0001***	0.240**	0.008**
LVMI (g/m^2)	0.343***	0.0001***	0.236**	0.009**

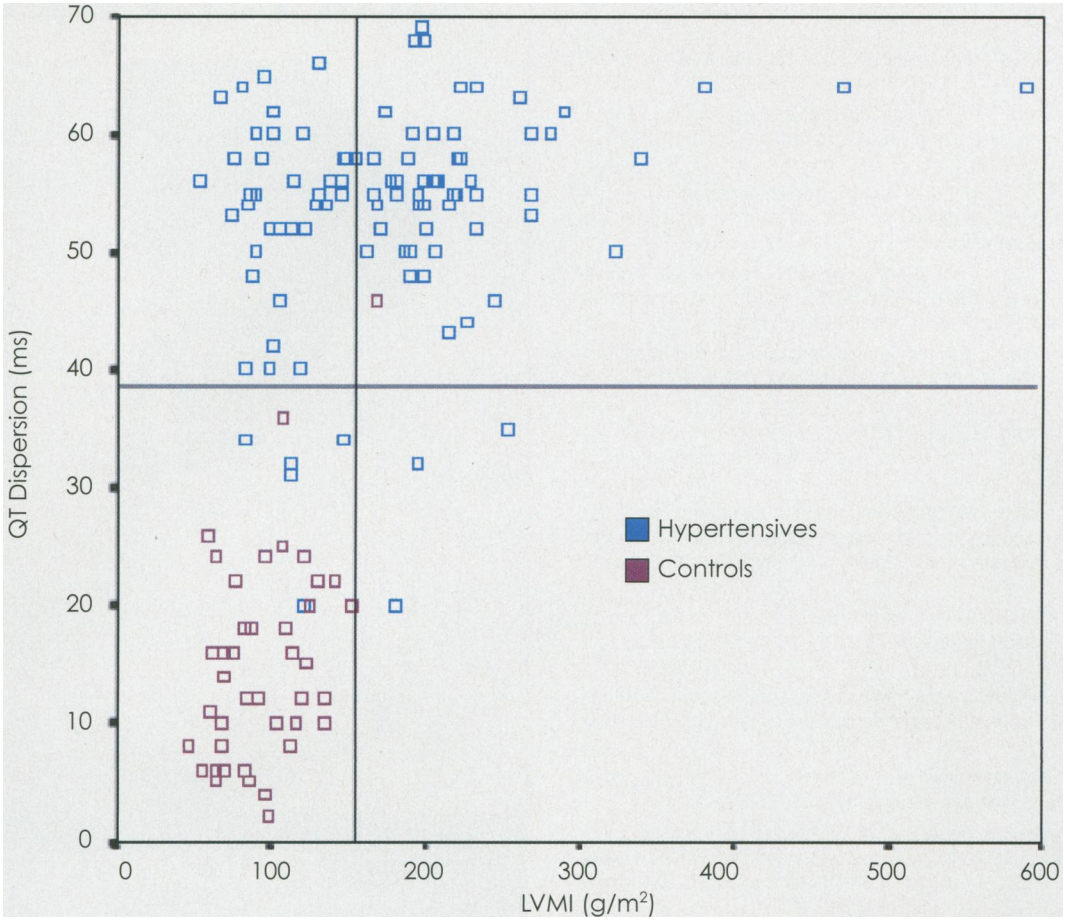
P value <0.05 (statistically significant); ECG LVH: electrocardiographic left ventricular hypertrophy; MAP: mean arterial pressure; IVSd: interventricular septum in diastole; LVIDd: left ventricular internal diameter in diastole; LVPWd: left ventricular posterior wall in diastole

Table 3. Variables in stepwise multiple linear regression analysis with significant correlation with QTD and adjusted QTD (ms)

Variable	QTD (ms)	P Value	Adjusted QTD (ms)	P Value
LVM (g)	0.225	0.005**	0.173	0.001**
LVMI (g/m^2)	0.131	0.004**	0.142	0.003**
SBP (mmHg)	0.145	0.003**	0.140	0.006**

All showed a significant p value (<0.05)

Figure 2. Relationship between QT dispersion (ms) and LVMI (g/m²)



persion of <39ms, and only about 29% of them without LVH had QT dispersion of >39 ms. This study, like others that measure QT dispersion manually, may contain all the inherent inter- and intraobserver defects of the method as a limitation. The use of automated computer algorithm with digital board is fairly more accurate for determination of QT dispersion. But, again, these facilities are lacking in a third-world country such as ours. Therefore, until the time these are provided by our government, we believe that the manually calculated QT dispersion may still be a simple, cheap and noninvasive method for detection of those hypertensives with an increased risk of sudden cardiac death.

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